

Amendments to the Specification:

Please insert the Abstract provided on a separate page attached hereto.

Please insert the enclosed sequence listing into the specification.

Page 41, lines 1-3, please replace this paragraph with the following amended paragraph:

HPW FFGKIPRAKA EEMLSKQRHD GAFLIRESES APGDFSLSVK
FGNDVQHFKV LRDGAGKYFL WVVKFNSLNE LVDYHRSTSV
SRNQQIFLRD IEQVPQQPT (SEQ ID NO:2)

Page 44, lines 21-29 and page 45, lines 1-3, please replace this paragraph with the following amended paragraph:

A sample of the purified and lyophilised Grb2-SH2 C-terminal hydrazide (100 µg) was treated with the protease Lys-C (5 µg) in 100mM ammonium bicarbonate buffer pH 8.2 (100 µL). After incubating at 30°C overnight the reaction was lyophilised and analysed by MALDI mass spectrometry. The observed mass of the C-terminal proteolytic fragment

(FNSLNELVDYHRSTSRSRNQQIFLRDIEQVPQQPTG) (SEQ ID NO:3)
(corresponds to that of the desired C-terminal hydrazide derivative (expected mass of C-terminal hydrazide proteolytic fragment 4229 Da; observed mass 4231 Da).

Page 45, lines 16-30 and page 46, lines 1-2, please replace this paragraph with the following amended paragraph:

Sequence of human MBP used:

MKIEEGKLVIWINGDKGYNGLAEVGKKFEKDTGIKV
TVEHPDKLEEKFPQVAATGDGPDIIFWAHDRFGGYA
QSGLLAEITPDFKAFAQDKLYPFTWDAVRYNGKLIAYPI
AVEALSLIYNKDLLPNPPKTWEEIPALDKELKAKGKS
ALMFNLQE PYFTWPLIAADGGYAFKYENGKYDIKDV
GV DNAGAKAGLTFLVDLIKKNHMNADTDYSIAEAAF
NKGETAMTINGPWAWSNIDTSKVNYGTVLPTFKGQ
PSKPFVGVL SAGINAASPNKELAKEFLENYLLTDEGL
EAVNKDKPLGAVALKS YEEELAKDPRIAATMENAQK
GEIMPNIPQMSAFWYAVRTAVINAASGRQTVD EALK
DAQTNSSSNNNNNNNNNL GIEGRGTLEG (SEQ ID NO:4)

Page 49, lines 14-30, please replace this paragraph with the following amended paragraph:

The inventors hypothesised that recombinant protein C-terminal hydrazides, generated by hydrazine treatment of the corresponding intein fusion precursor, can be site-specifically modified by chemoselective ligation with aldehyde and ketone containing peptides and labels. To demonstrate such an approach, the ability of a synthetic ketone containing peptide to ligate with the Grb2-SH2 C-terminal hydrazide generated above was investigated. A synthetic peptide corresponding to the c-myc epitope sequence was synthesised GEQKLISEEDL-NH₂ (SEQ ID NO:6), whereby pyruvic acid was coupled to the amino terminus of the peptide as the last step of the assembly. This peptide (designated CH₃COCO-myc) was purified to > 95% purity by RPHPLC and lyophilised (ESMS expected monoisotopic mass 1328.6 Da; observed mass 1328.6 Da).

Page 52, lines 1-16, please replace this paragraph with the following amended paragraph:

To establish the reactivity of CH₃COCO-Lys(Fl) with C-terminal hydrazide peptides and proteins, the reaction of CH₃COCO-Lys(Fl) with a small synthetic C-terminal hydrazide peptide SLAYG-NHNH₂ (SEQ ID NO:5-NHNH₂) was investigated. A sample of CH₃COCO-Lys(Fl) and SLAYG-NHNH₂ peptide were co-dissolved in 100 mM sodium acetate buffer pH 4.5 to give final concentrations of 0.3 mM and 2 mM respectively. After 20 h incubation at room temperature, the reaction was deemed complete as determined by RPHPLC analysis. All the starting CH₃COCO-Lys(Fl) had reacted to give predominantly a single product. The mass of which corresponds to the desired ligation product, namely conjugation of the two reactants via hydrazone bond formation (ESMS expected monoisotopic mass 1079 Da; observed mass 1080 Da).